

REMARKS

Claims 1-12 and 15-59 are pending. Claims 13 and 14 have been cancelled. Claims 1-11, 16-31, 33-51 and 57 have been withdrawn from consideration. Applicants reserve the right to file one or more divisional applications directed to the subject matter of the non-elected claims.

The amendments to the pending claims are made to more clearly define the inventions. It is submitted that the amendments introduce no new matter and entry of the same is respectfully requested. By these amendments, the Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which the Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997).

I. Rejection of claims 12-15, 32 and 52 under 35 U.S.C. § 102(b) as anticipated by Tuck et al.

The Examiner rejected claims 12-15, 32 and 52 under 35 U.S.C. § 102(b). Specifically, the Examiner alleges that these claims are "anticipated by Tuck et al. (Blood (1994) 84(7); 21-82-2188." Paper No. 19 at page 2. Applicants respectfully traverse.

To support an anticipation rejection under 35 U.S.C. § 102(b), the Examiner must demonstrate that each and every element of a claimed invention is disclosed within a single prior art reference. *In re Bond*, 15 U.S.P.Q.2d 1566, 1567 (Fed. Cir. 1990). In other words, to anticipate the claim must encompass and empower a patentee or assignee to exclude others from making, using, or selling a product described in said printed publication. *Helifix Ltd. v. Blok-Lok Ltd.*, 54 U.S.P.Q.2d 1299, 1304 (Fed. Cir. 2000). Indeed, the printed publication must describe an applicant's claimed invention sufficiently to have placed a person of ordinary skill in the art in the field of the invention in possession of it. *See generally In re Paulson*, 31 U.S.P.Q.2d 1671 (Fed. Cir. 1994).

Without acquiescing to the propriety of the Examiner's rejection and in order to facilitate prosecution of the pending application, Applicants have amended claim 12 by combining the claim with the subject matter of claim 53, now deleted. Specifically, Applicants have amended claim 12 to specify the isolated membrane vesicles comprise one or more recombinant class II molecules of the major histocompatibility complex.

Applicants have amended claim 15 to specify that the vesicles further comprise (in addition to recombinant class II molecules of the major histocompatibility complex) a heterologous molecule of interest selected from the group consisting of a molecule of the major histocompatibility complex, an antigen, a receptor ligand, a ligand receptor, a nucleic acid, a pharmacological product, a tracer, and a purification peptide.

Applicants have amended claim 52 to recite the new wording of claims 12 and 15 and claim 52 now refers to claim 15 (instead of claim 12).

With respect to the cited reference, Tuck relates to the expression of M-CSF in COS-1 cells and vesicles derived from such cells. The Examiner states that “Tuck does not specifically teach that the isolated vesicles are mastocyte-derived” and “Tuck et al does not specifically teach recombinant MHC Class II molecules of the DR1 serotype.” Paper No. 19 at pages 2 and 4, respectively. Applicants respectfully disagree.

Applicants submit that the only recombinant protein mentioned and expressed in the COS-1 cells of Tuck is M-CSF. Tuck neither describes a COS-1 cell expressing a recombinant MHC Class II molecule nor an isolated membrane vesicle secreted by a COS-1 cell expressing a recombinant MHC Class II molecule. Therefore, nowhere does Tuck teach or suggest an isolated membrane vesicle wherein the vesicle is secreted from a mastocyte or mastocyte derived cell, which comprises one or more recombinant class II molecules of the major histocompatibility complex. Moreover, Tuck does not teach or suggest an isolate membrane vesicle that further comprises a heterologous molecule of interest selected from the group consisting of a molecule of the major histocompatibility complex, a receptor ligand, a ligand receptor, a nucleic acid, a pharmacological product, a tracer, and a purification peptide, where the heterologous molecule may be present on the surface of the vesicle.

Accordingly, because Tuck does not teach each and every element of the claimed inventions, claims 12-15, 32 and 52 are not anticipated under 35 U.S.C. § 102(b). Accordingly, Applicants respectfully request that the present rejection be reconsidered and withdrawn.

II. Rejection of Claim 12, 53-56, 58 and 59 under 35 U.S.C. § 103(a) over Tuck in view of Xu

The Examiner rejected claims 12, 53-56, 58 and 59 under 35 U.S.C. § 103(a). Paper No. 19 at page 4. Specifically, the Examiner alleges that these claims are “unpatentable over Tuck et al., (Blood (1994) 84(7); 2182-2188 . . . in view of Xu (Molec. Immunol. (1994)

21(10):723-731)." *Id.* Applicants respectfully traverse.

To maintain a proper rejection under 35 U.S.C. § 103, the USPTO must meet four conditions to establish a *prima facie* case of obviousness. First, the USPTO must show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the USPTO must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the USPTO must show the suggestion, teaching, or motivation to combine the prior art references. *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999).

Without acquiescing to the propriety of the Examiner's rejection and in order to facilitate prosecution of the pending application, Applicants have amended claim 12 (see above). Applicants have deleted claim 53. Applicants have amended claims 54-56 to depend from amended claim 12. Those claims previously depended from claim 53, now deleted. Applicants also amended claim 58 to depend from amended claim 12 and to correct a typographical error. Specifically, claim 58 now refer to recombinant class II molecule of the major histocompatibility complex.

With respect to the rejection, the Examiner alleges that "it would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Xu regarding the recombinant expression of DR1 α and β chains with the teachings of Tuck to study the interaction of vesicle-bound MHC molecules with effector CD4+ T cells." *Id.* at page 4. Applicants assert that Tuck is deficient as a primary reference as discussed above in Applicants traversal of the §102. Applicants further assert that Xu, as a secondary reference, does not remedy the deficiencies of Tuck.

Specifically, the Examiner alleges that "Xu does teach the successful recombinant expression of MHC class II in COS-1 cells." As mentioned in the previous Reply, Xu describes the recombinant expression of HLA DR1 α and β chains in COS-1 cells. Xu states that "MHC class II molecules bind intracellularly process, immunogenic peptides in post-Golgi/endosomal compartments [of COS-1 cells] and transport them to the cell surface for the presentation to T lymphocytes." Nowhere, however, does Xu describe membrane vesicles

expressing recombinant MHC class II molecules. Further, nowhere does Xu describe membrane vesicles according to the invention secreted by a mastocyte or mastocyte-derived cells.

The Examiner further alleges “Tuck teaches that membrane fragments, such as vesicles, can express functional MHC class II molecules and Xu teaches that functional MHC class II can be expressed in COS-1 cells. Accordingly, the combined teachings would have provided the artisan with the information needed to create recombinant MHC class II-bearing vesicles from COS-1 cells.” Applicants disagree and note that such an allegation is the result of improper hindsight reconstruction. *See In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988). As explained above, Tuck does not teach or suggest that membrane fragments, such as vesicles, can express recombinant MHC class II molecules. Indeed, M-CSF is the only protein recombinantly expressed in COS-1 cells in the Tuck reference.

Furthermore, M-CSF and MHC class II molecules are of a different nature—M-CSF is a soluble protein while MHC class II molecules are membrane proteins. One of ordinary skill in the art would have found no motivation in Tuck to express a membranous protein in a membrane vesicle. Furthermore, one of ordinary skill in the art would have found no motivation in Xu to express a recombinant MHC class II molecule in a membrane vesicle.

Indeed, Applicants are the first to demonstrate that membrane vesicles secreted from a mastocyte or mastocyte derived cell are able to express functional recombinant MHC class II molecules. The expression of a particular functional recombinant molecule in or on the surface of membrane vesicles secreted from a particular type of cell, followed by the isolation of vesicles expressing said functional recombinant molecule are not trivial. One of ordinary skill in the art would not have found in Tuck a reasonable expectation of success. In fact, as stated in Tuck, “[d]epending on the cellular origin of extracellular vesicles, diverse functions are mediated by the shedding process . . . Whether a subset of vesicles shed from COS cells transfected with cDNA for M-CSF expresses the activity (analogous to mBPA expression by MHC class-II antigen –bearing vesicles) or whether all shed vesicles express activity is unknown.” Tuck et al., p. 2816 (emphasis added).

Therefore, Tuck, either alone or in combination with Xu, does not support a rejection under 35 U.S.C. § 103. Therefore, the Examiner has failed to establish a *prima facie* case of obviousness under 35 U.S.C. § 103. Applicants respectfully request that the present rejection be reconsidered and withdrawn.

CONCLUSION

Applicants have properly and fully addressed each of the Examiner's grounds for rejection. Applicants submit that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited.

If there are any additional fees due in connection with the filing of this amendment, please charge the fees to undersigned's Deposit Account No. 50-1067. If any extensions or fees are not accounted for, such extension is requested and the associated fee should be charged to our deposit account.

Respectfully submitted,



Don J. Peto
Reg. No. 33,754

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Preston Gates Ellis & Rouvelas Meeds LLP
1735 New York Avenue, NW, Suite 500
Washington, DC 20006
Telephone: (202) 628-1700
Facsimile: (202) 331-1024